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NEWS 7	Sep 03	JAPIO has been reloaded and enhanced
NEWS 8	Sep 16	Experimental properties added to the REGISTRY file
NEWS 9	Sep 16	CA Section Thesaurus available in CAPLUS and CA
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Patel <5/24/2003>

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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STRUCTURE FILE UPDATES: 22 MAY 2003 HIGHEST RN 519137-84-9
DICTIONARY FILE UPDATES: 22 MAY 2003 HIGHEST RN 519137-84-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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L1 STRUCTURE UPLOADED

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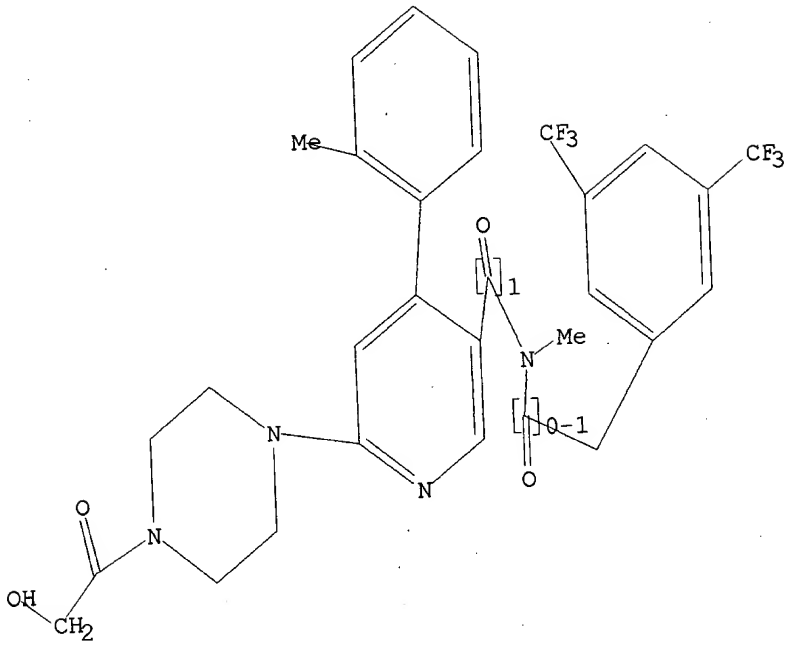
L1 STR



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SAMPLE SEARCH INITIATED 08:31:55 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

0 ANSWERS

100.0% PROCESSED 1 ITERATIONS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**

PROJECTED ITERATIONS: 1 TO 80
PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=> s l1 sss full
FULL SEARCH INITIATED 08:32:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6 TO ITERATE

1 ANSWERS

100.0% PROCESSED 6 ITERATIONS
SEARCH TIME: 00.00.01

L3 1 SEA SSS FUL L1

=> file caplus
COST IN U.S. DOLLARS

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FULL ESTIMATED COST	148.15	148.36

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FILE COVERS 1907 - 24 May 2003 VOL 138 ISS 22
FILE LAST UPDATED: 23 May 2003 (20030523/ED)

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=> s l3
L4 3 L3

=> d l3 fbib hitstr abs total
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YOU HAVE REQUESTED DATA FROM FILE 'REGISTRY' - CONTINUE? (Y)/N:N

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L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 2003:57902 CAPLUS
DN 138:117662
TI Use of NK-1 receptor antagonists for the treatment of brain, spinal or nerve injury
IN Hoffmann, Torsten; Nimmo, Alan John; Sleight, Andrew; Vankan, Pierre; Vink, Robert
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003006016	A2	20030123	WO 2002-EP7323	20020703

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

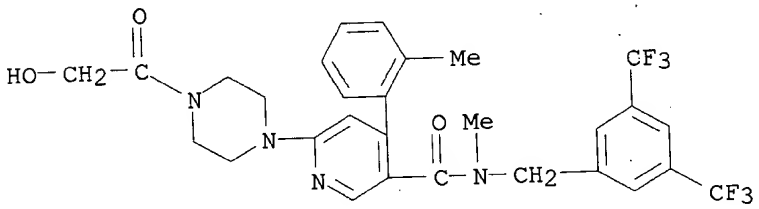
US 2003083345 A1 20030501 EP 2001-116812 A 20010710
US 2002-187587 20020702
EP 2001-116812 A 20010710

OS MARPAT 138:117662

IT **401891-32-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NK-1 receptor antagonist for treatment of brain, spinal or nerve injury)

RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



AB The invention discloses the use of an NK-1 receptor antagonist (Markush included), e.g. N-(3,5-bis-trifluoromethylbenzyl)-N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide, optionally in combination with a magnesium salt, for the treatment and/or prevention of brain, spinal or nerve injury. The invention also relates to pharmaceutical compns. comprising one or more such NK-1 receptor antagonists, optionally in combination with a magnesium salt, and a pharmaceutically acceptable excipient, for the treatment and/or prevention of brain, spinal or nerve injury.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

AN 2002:832668 CAPLUS

DN 137:337901

TI Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia

IN Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; Sleight, Andrew John; Vankan, Pierre

PA F. Hoffmann-La Roche A.-G., Switz.

SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

PI WO 2002085458 A2 20021031 WO 2002-EP1085 20020202
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
EP 2001-109853 A 20010423

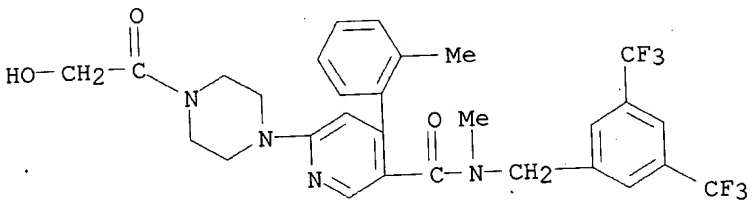
US 2003004157 A1 20030102 US 2002-71570 20020208
EP 2001-109853 A 20010423

OS MARPAT 137:337901

IT **401891-32-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia)

RN 401891-32-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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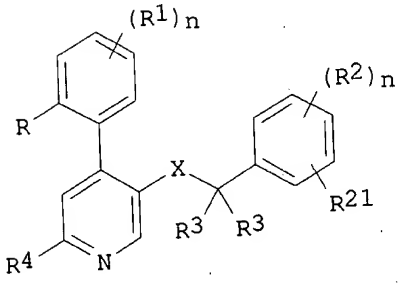


I

AB Use of an NK-1 receptor antagonist for the treatment or prevention of benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1 receptor antagonists are compds. of the general formula [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H , halo , CF3, alkyl, alkoxy, cyano; R2R21 = CH:CHCH:CH, optionally substituted by 1-2 alkyl, halo, alkoxy; R3 = H, alkyl; R3R3C = cycloalkyl; R4 = H,

N(R5)2, NR5(CH2)nOH, cyclic tertiary amine, etc.; X = CONR5, (CH2)pO, NR5(CH2)p, etc.; R5 = H, cycloalkyl, Ph, PhCH2, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1.lambda.6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.lambda.6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (prepn. given) oxone were stirred 2 days at room temp. to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.lambda.6-thiomorpholin-4-yl)-4-o-tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate wt. by 58% after 39 wk.

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS
AN 2002:157739 CAPLUS
DN 136:216651
TI Preparation of 4-phenylpyridines as neurokinin-1 receptor antagonists
IN Godel, Thierry; Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

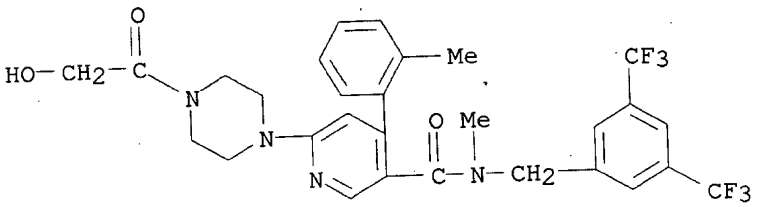
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002016324	A1	20020228	WO 2001-EP8686	20010727
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
				EP 2000-117003 A	20000808
	AU 2002012118	A5	20020304	AU 2002-12118	20010727
				EP 2000-117003 A	20000808
				WO 2001-EP8686 W	20010727
	EP 1309559	A1	20030514	EP 2001-980219	20010727
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
				EP 2000-117003 A	20000808
				WO 2001-EP8686 W	20010727
	US 2002040040	A1	20020404	US 2001-922066	20010803
				EP 2000-117003 A	20000808
	NO 2003000632	A	20030207	NO 2003-632	20030207
				EP 2000-117003 A	20000808
				WO 2001-EP8686 W	20010727

OS MARPAT 136:216651
IT **401891-32-5P**

Patel <5/24/2003>

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 401891-32-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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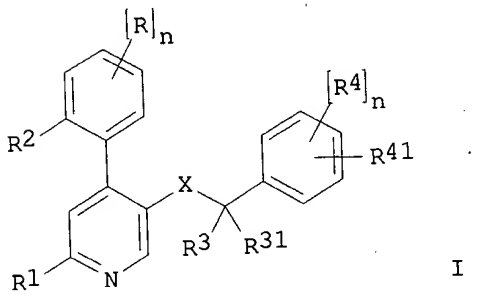

I

AB The title compds. [I; R = H, halo; R1 = (C.tplbond.C)mR11, (CR'=CR'')mR11 (wherein R11 = halo, CN, aryl, etc.; R', R'' = H, OH, alkyl, etc.); R2 = H, alkyl, alkoxy, halo, CF3; R3, R31 = H, alkyl or form together with the C atom to which they are attached a cycloalkyl group; R4, R41 = H, halo, CF3, alkyl, alkoxy; R and R2 or R4 and R41 may be together CH=CHCH=CH, optionally substituted by one or two substituents selected from alkyl, halo or alkoxy; X = CONR8, (CH2)pO, (CH2)pNR8, NR8CO, NR8(CH2)p (wherein R8 = H, alkyl); n = 1-2; m = 0-4; p = 1-2] which are antagonists of the Neurokinin 1 (NK-1, substance P) receptor, and therefore useful in the treatment of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R = H; R1 = N(OH)CH2CH2OH; R2 = Me; R3, R31 = Me; R4 = 3-CF3; R41 = 5-CF3; X = NMeCO] which showed pKi of 9.29 in human NK1 receptor assay, was given.

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SEARCH CHARGES	12.96	12.96
DISPLAY CHARGES	---	---
	13.76	162.12
	0.68	0.68
CAPLUS FEE (5%)	---	---
	14.44	162.80
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NEWS 36	May 05	Pharmacokinetic information and systematic chemical names added to PHAR
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Patel <5/24/2003>

NEWS 40 May 19 Simultaneous left and right truncation added to WSCA
NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003
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	SINCE FILE ENTRY	TOTAL SESSION
COST IN U.S. DOLLARS		
FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 22 MAY 2003 HIGHEST RN 519137-84-9
DICTIONARY FILE UPDATES: 22 MAY 2003 HIGHEST RN 519137-84-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

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Patel <5/24/2003>

L1 STRUCTURE UPLOADED

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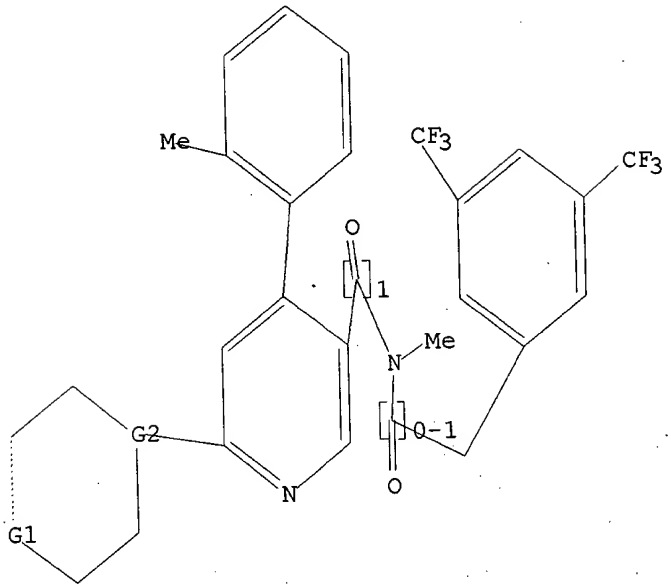

G1 C,O,N
G2 C,N

Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 8 TO ITERATE

100.0% PROCESSED 8 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 8 TO 329
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

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SEARCH TIME: 00.00.01

L3 39 SEA SSS FUL L1

Patel <5/24/2003>

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                                                 ENTRY    SESSION
FULL ESTIMATED COST                             148.15     148.36

FILE 'CAPLUS' ENTERED AT 08:43:57 ON 24 MAY 2003
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 24 May 2003  VOL 138 ISS 22
FILE LAST UPDATED: 23 May 2003  (20030523/ED)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.

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L4            7 L3

=> s l4 fbib hitstr abs total
MISSING OPERATOR L4 FBIB
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

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L4   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2003 ACS
AN   2003:57902  CAPLUS
DN   138:117662
TI   Use of NK-1 receptor antagonists for the treatment of brain, spinal or
     nerve injury
IN   Hoffmann, Torsten; Nimmo, Alan John; Sleight, Andrew; Vankan, Pierre;
     Vink, Robert
PA   F. Hoffmann-La Roche A.-G., Switz.
SO   PCT Int. Appl., 36 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG

US 2003083345 A1 20030501

EP 2001-116812 A 20010710
US 2002-187587 20020702
EP 2001-116812 A 20010710

OS MARPAT 138:117662

IT **290296-84-3 290296-85-4 290296-86-5**
290296-89-8 290296-93-4 290296-94-5
290296-95-6 290296-96-7 290296-98-9
290296-99-0 290297-00-6 290297-57-3
391674-85-4 391674-86-5 391674-90-1
391675-01-7 393508-72-0 393508-73-1
401891-32-5 401891-35-8 401891-70-1
401892-63-5 474026-12-5
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(NK-1 receptor antagonist for treatment of brain, spinal or nerve injury)

RN 290296-84-3 CAPLUS
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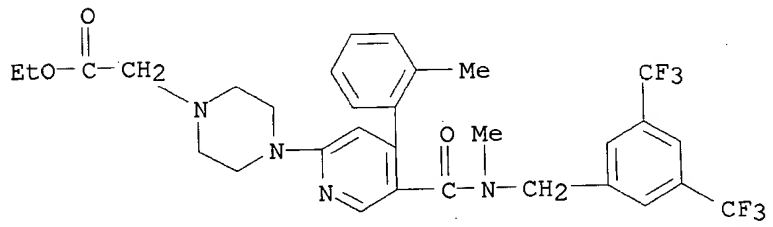

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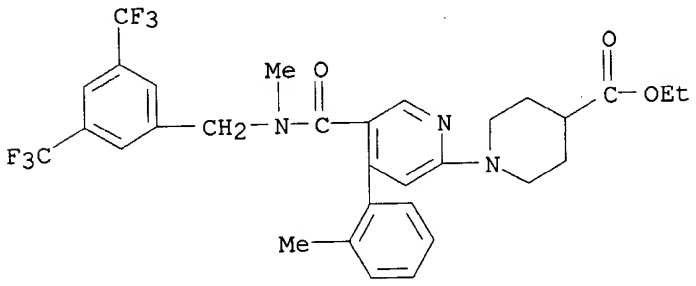

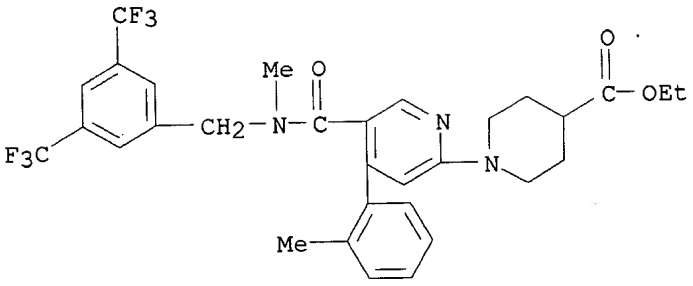

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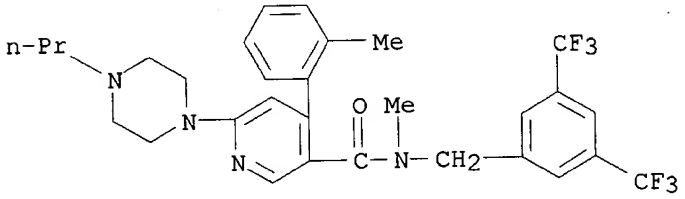

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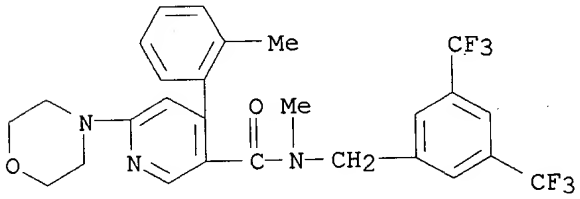

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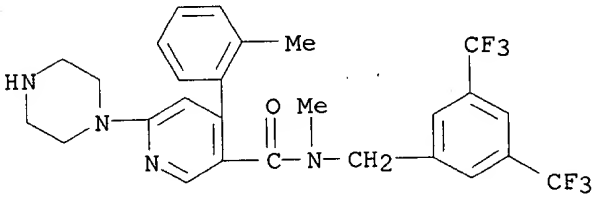

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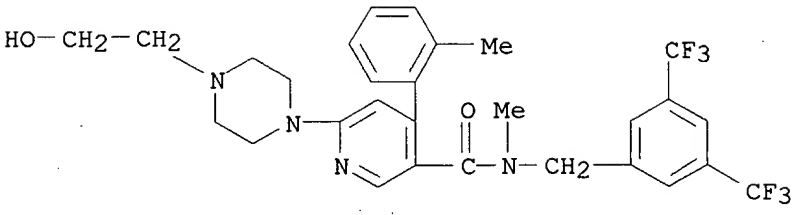
NAME)



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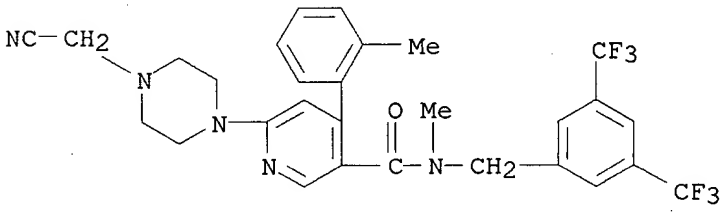

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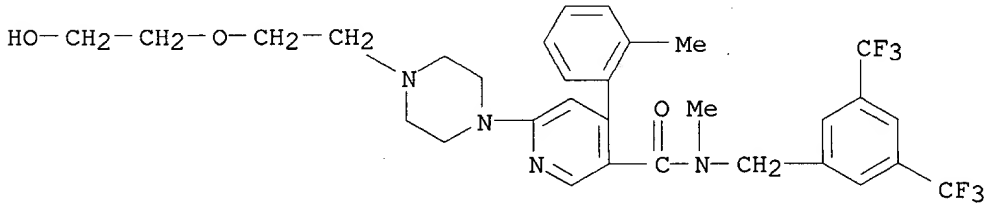
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



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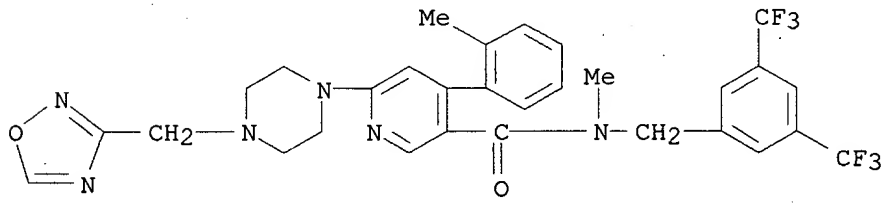

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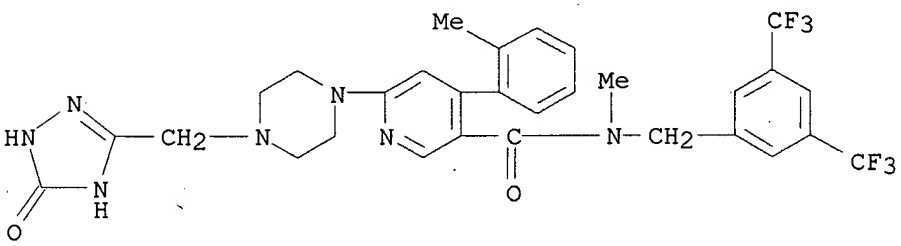

RN 290297-00-6 CAPLUS
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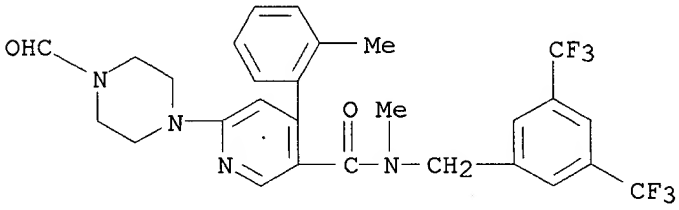

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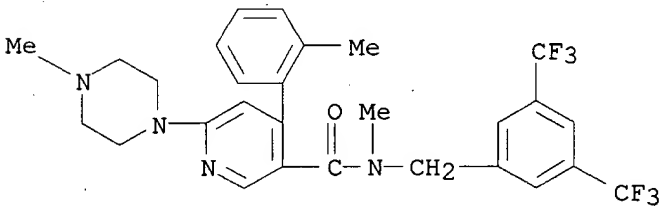
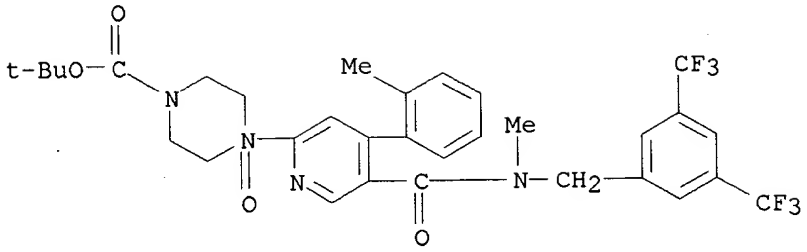
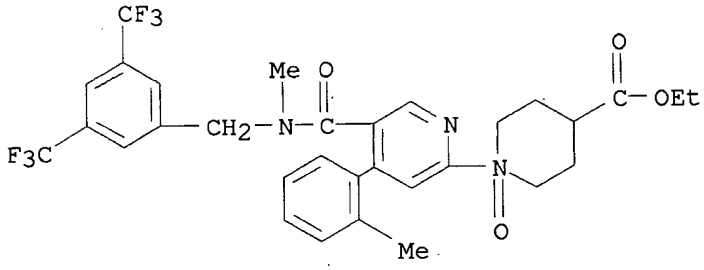


RN 391674-85-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester, 4-oxide (9CI) (CA INDEX NAME)



RN 391674-86-5 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester, 1-oxide (9CI) (CA INDEX NAME)



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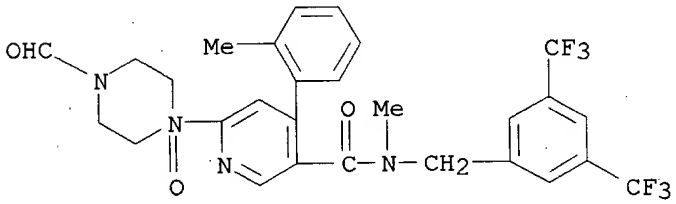
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-oxido-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 391675-01-7 CAPLUS
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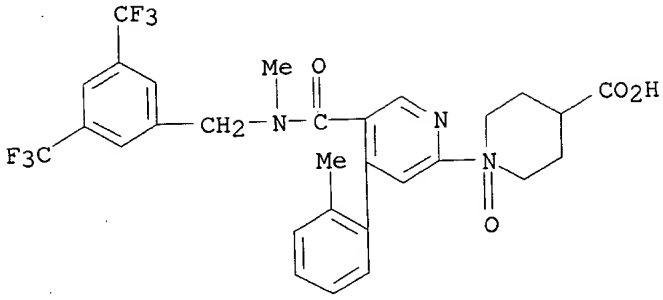

RN 393508-72-0 CAPLUS
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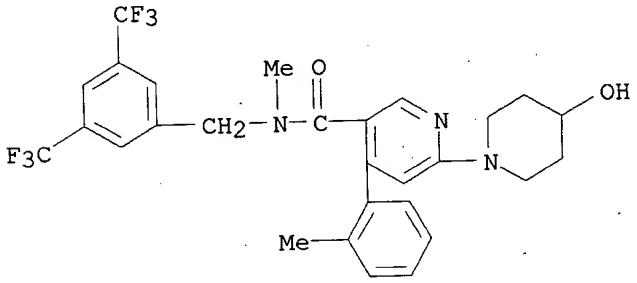
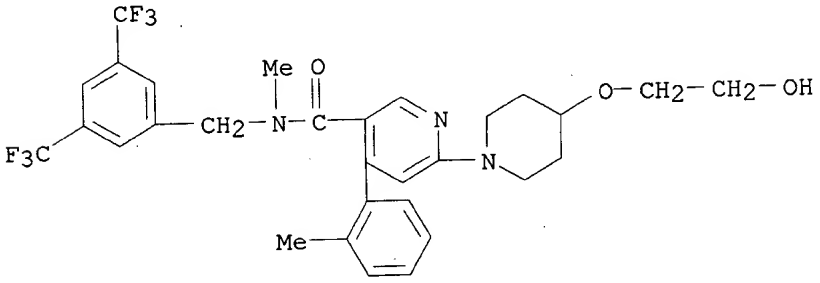
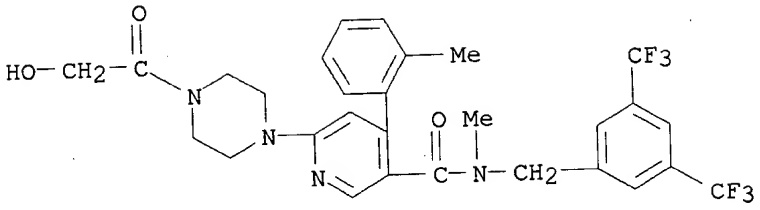


RN 393508-73-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethoxy)-1-piperidinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401891-32-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401891-35-8 CAPLUS
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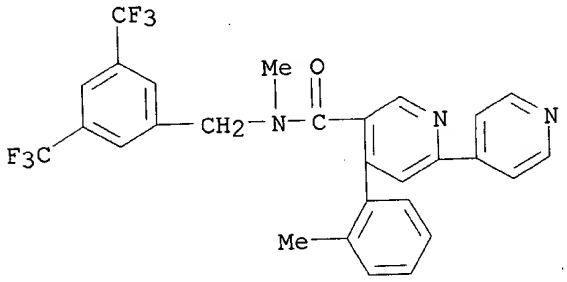
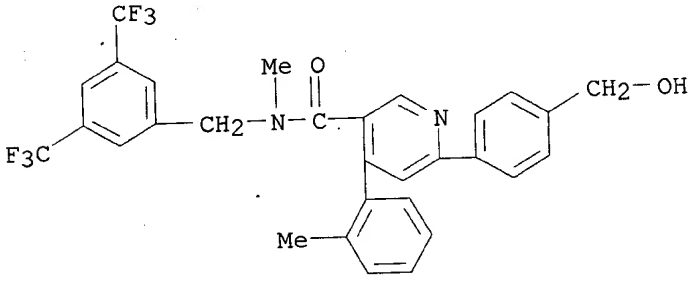
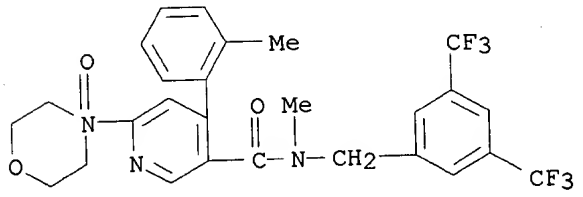


RN 401891-70-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxymethyl)phenyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401892-63-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 474026-12-5 CAPLUS
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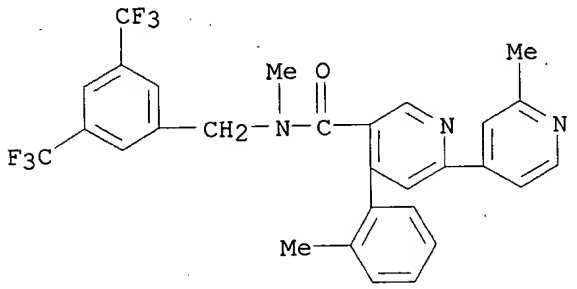

AB The invention discloses the use of an NK-1 receptor antagonist (Markush included), e.g. N-(3,5-bis-trifluoromethylbenzyl)-N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide, optionally in combination with a magnesium salt, for the treatment and/or prevention of brain, spinal or nerve injury. The invention also relates to pharmaceutical compns. comprising one or more such NK-1 receptor antagonists, optionally in combination with a magnesium salt, and a pharmaceutically acceptable excipient, for the treatment and/or prevention of brain, spinal or nerve injury.

L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2002:832668 CAPLUS
DN 137:337901
TI Preparation and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia
IN Buser, Susanne; Ford, Anthony P. D. W.; Hoffmann, Torsten; Lenz, Barbara; Sleight, Andrew John; Vankan, Pierre
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

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PI	WO 2002085458	A2	20021031	WO 2002-EP1085	20020202
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OS MARPAT 137:337901
IT **290296-86-5 290296-89-8 290296-93-4**

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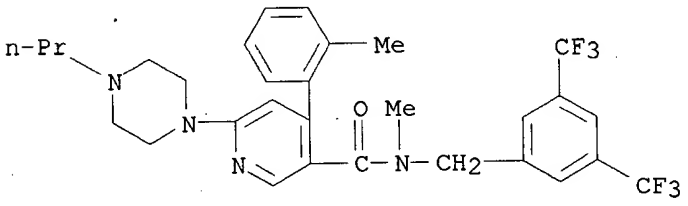
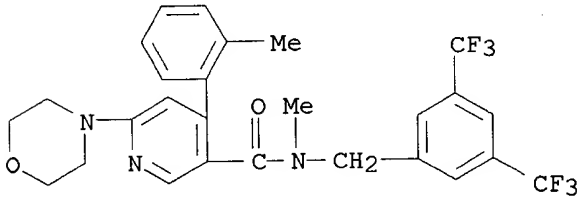
393508-73-1 401891-32-5 401891-35-8
401891-70-1 401892-63-5 474026-12-5
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. and use of amides as NK-1 receptor antagonists against benign prostatic hyperplasia)

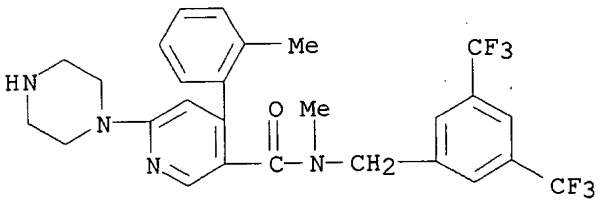
RN 290296-86-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-propyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



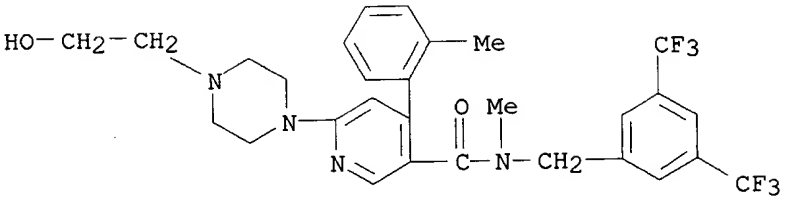
RN 290296-89-8 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



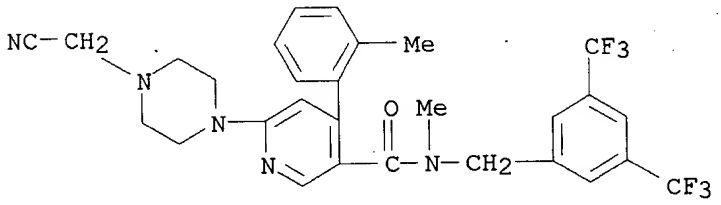
RN 290296-93-4 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



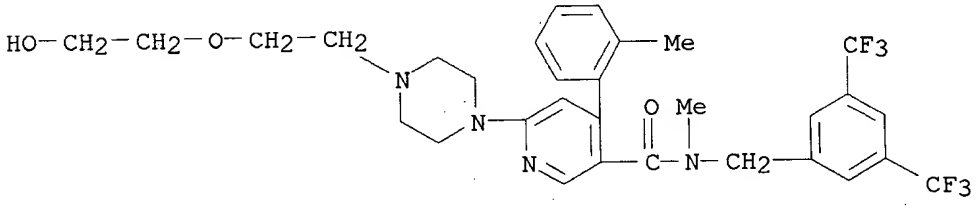
RN 290296-94-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



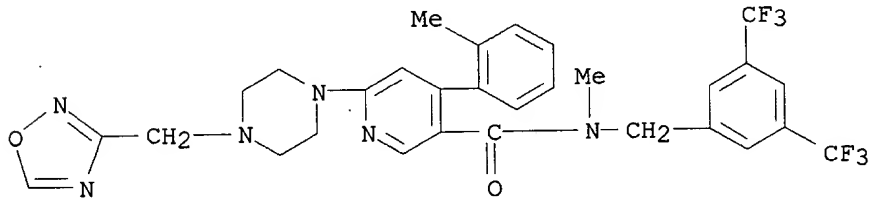
RN 290296-95-6 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(cyanomethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 290296-96-7 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

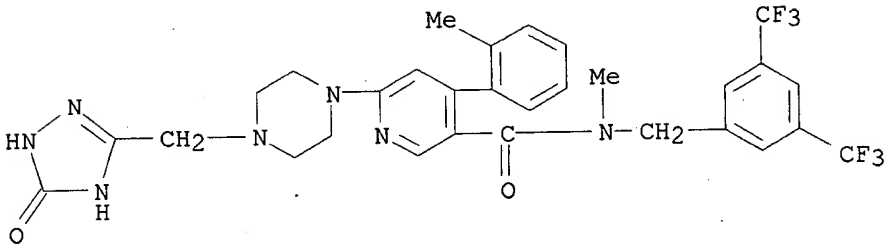


RN 290296-98-9 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-[4-(1,2,4-oxadiazol-3-ylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

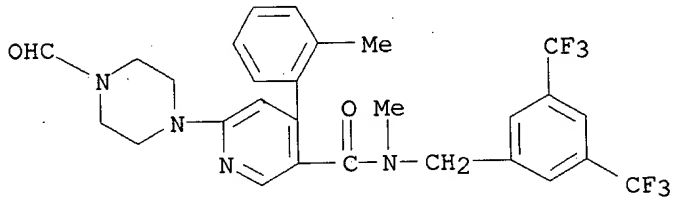


RN 290296-99-0 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-

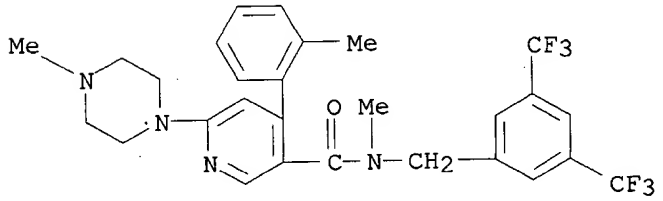
[(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)methyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



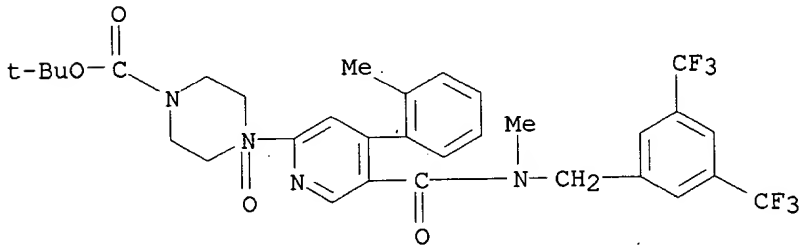
RN 290297-00-6 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

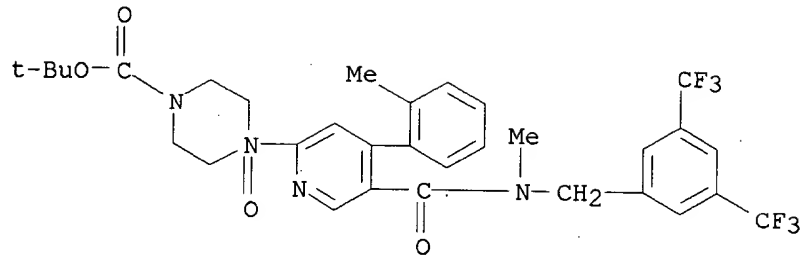


RN 290297-57-3 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

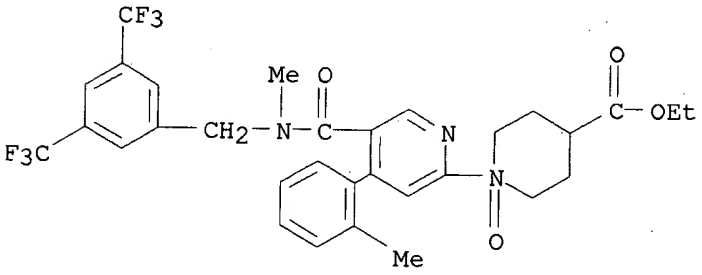


RN 391674-85-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester, 4-oxide (9CI) (CA INDEX NAME)

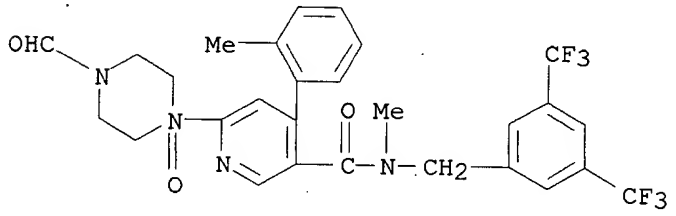




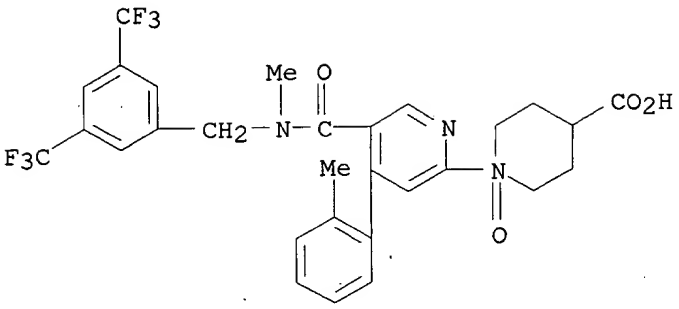
RN 391674-86-5 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester, 1-oxide (9CI) (CA INDEX NAME)



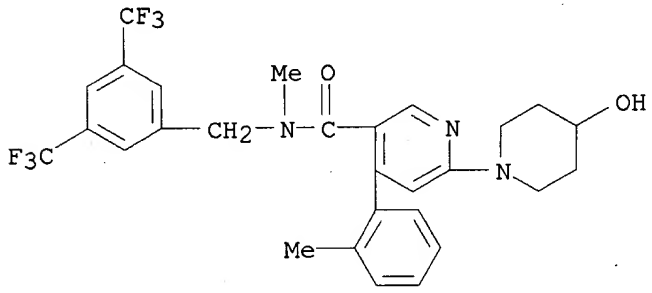
RN 391674-90-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-oxido-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



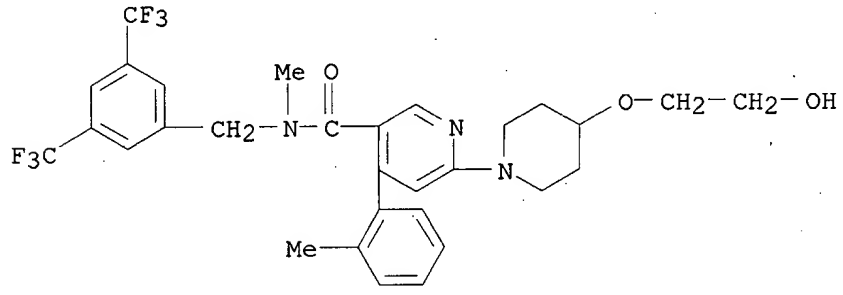
RN 391675-01-7 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1-oxide (9CI) (CA INDEX NAME)



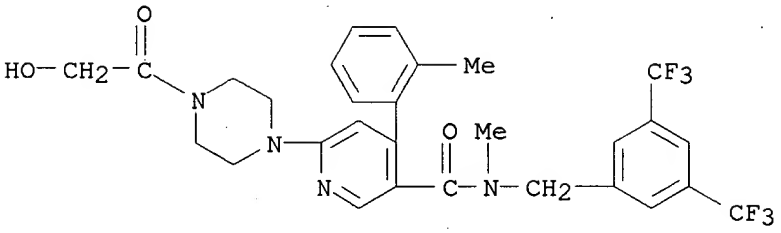
RN 393508-72-0 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-hydroxy-1-piperidinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



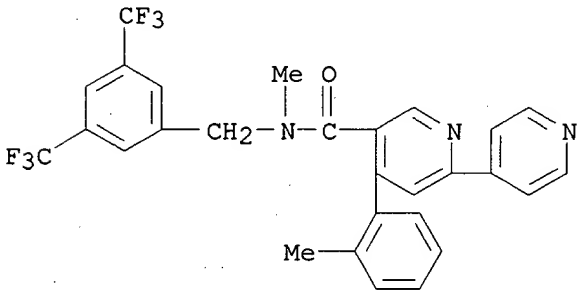
RN 393508-73-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethoxy)-1-piperidinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



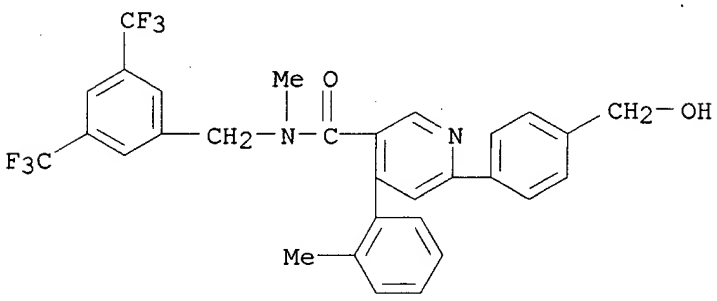
RN 401891-32-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



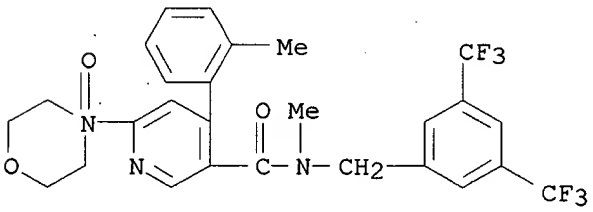
RN 401891-35-8 CAPLUS
CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



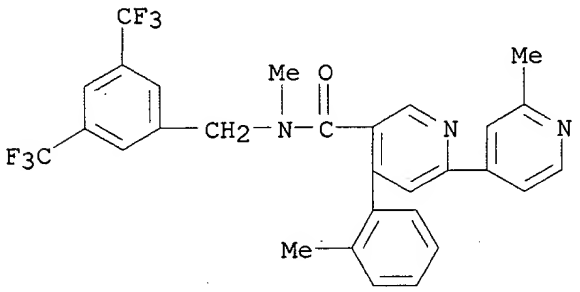
RN 401891-70-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxymethyl)phenyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



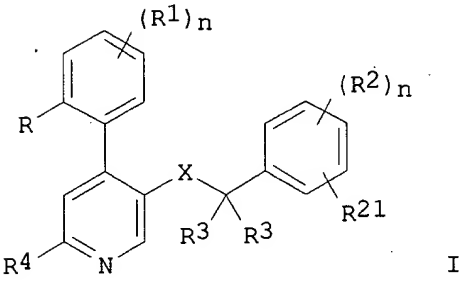
RN 401892-63-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 474026-12-5 CAPLUS
CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N,2'-dimethyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



GI



I

AB Use of an NK-1 receptor antagonist for the treatment or prevention of benign prostatic hyperplasia (BPH) is claimed. The preferred NK-1 receptor antagonists are compds. of the general formula [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H , halo , CF3, alkyl, alkoxy, cyano; R2R21 = CH:CHCH:CH, optionally substituted by 1-2 alkyl, halo, alkoxy; R3 = H, alkyl; R3R3C = cycloalkyl; R4 = H, N(R5)2, NR5(CH2)nOH, cyclic tertiary amine, etc.; X = CONR5, (CH2)pO, NR5(CH2)p, etc.; R5 = H, cycloalkyl, Ph, PhCH2, alkyl; n = 0-4; p = 1-3]. Preferred compds. are 2-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-(6-morpholin-4-yl-4-o-tolyl-pyridin-3-yl)isobutyramide, 3-(3,5-bis-trifluoromethyl-phenyl)-N-methyl-N-[6-(4-methyl-piperazin-1-yl)-4-o-tolyl-pyridin-3-yl]isobutyramide, 2-(3,5-bis-trifluoromethyl-phenyl)-N-[6-(1,1-dioxo-1.lambda.6-thiomorpholin-4-yl)-4-o-tolyl-pyridin-3-yl]-N-methylisobutyramide, and 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.lambda.6-thiomorpholin-4-yl)-4-(4-fluoro-2-methyl-phenyl)-pyridin-3-yl]-N-methylisobutyramide. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-(6-thiomorpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide (prepn. given) oxone were stirred 2 days at room temp. to give 2-(3,5-bis-trifluoromethylphenyl)-N-[6-(1,1-dioxo-1.lambda.6-thiomorpholin-4-yl)-4-o-tolylpyridin-3-yl]-N-methylisobutyramide. 2-(3,5-Bistrifluoromethylphenyl)-N-methyl-N-methyl-N-(6-morpholin-4-yl-4-o-tolylpyridin-3-yl)isobutyramide at 60 mg/kg/day orally in dogs reduced prostate wt. by 58% after 39 wk.

L4 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2002:157739 CAPLUS
DN 136:216651
TI Preparation of 4-phenylpyridines as neurokinin-1 receptor antagonists
IN Godel, Thierry; Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002016324	A1	20020228	WO 2001-EP8686	20010727
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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				EP 2000-117003 A	20000808
	AU 2002012118	A5	20020304	AU 2002-12118	20010727
				EP 2000-117003 A	20000808
				WO 2001-EP8686 W	20010727
	EP 1309559	A1	20030514	EP 2001-980219	20010727
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				WO 2001-EP8686 W	20010727
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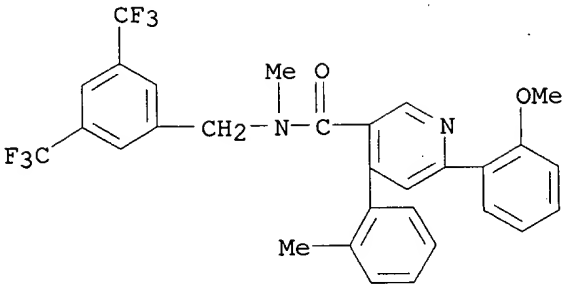
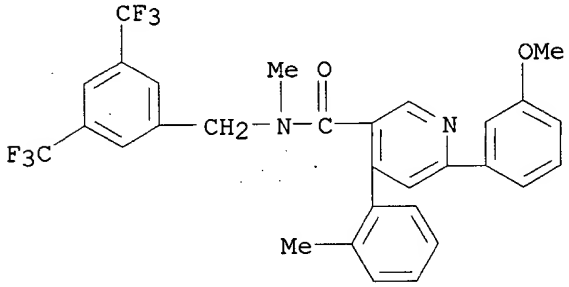
				EP 2000-117003 A	20000808
	NO 2003000632	A	20030207	NO 2003-632	20030207
				EP 2000-117003 A	20000808
				WO 2001-EP8686 W	20010727

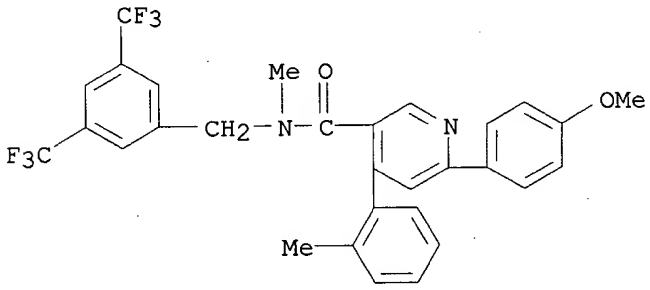
OS MARPAT 136:216651
IT **401891-47-2P 401891-48-3P 401891-49-4P**
401891-69-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)
RN 401891-47-2 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(2-methoxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



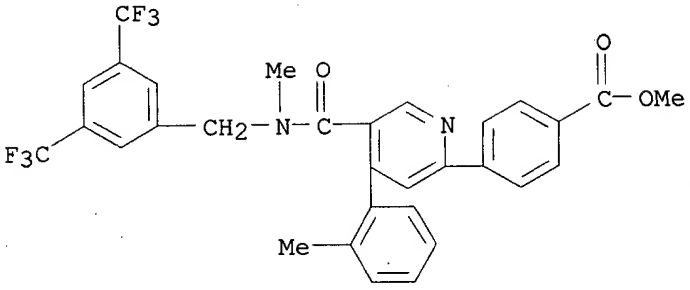
RN 401891-48-3 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(3-methoxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401891-49-4 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-methoxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

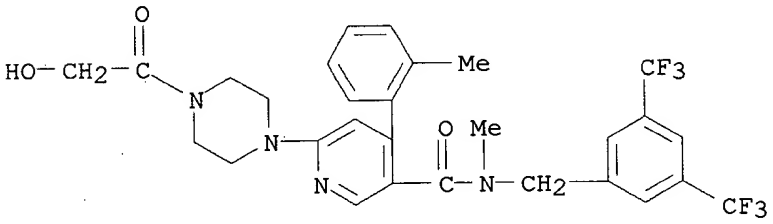


RN 401891-69-8 CAPLUS
CN Benzoic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, methyl ester (9CI) (CA INDEX NAME)

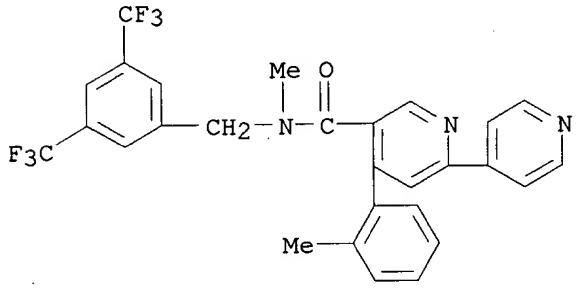


IT **401891-32-5P 401891-35-8P 401891-50-7P 401891-51-8P 401891-52-9P 401891-70-1P 401891-71-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

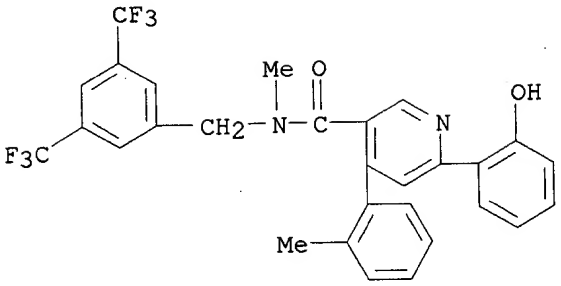
RN 401891-32-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxyacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



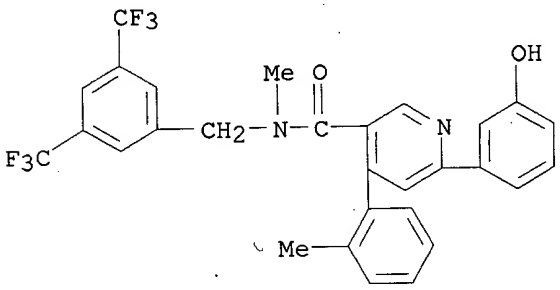
RN 401891-35-8 CAPLUS
CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



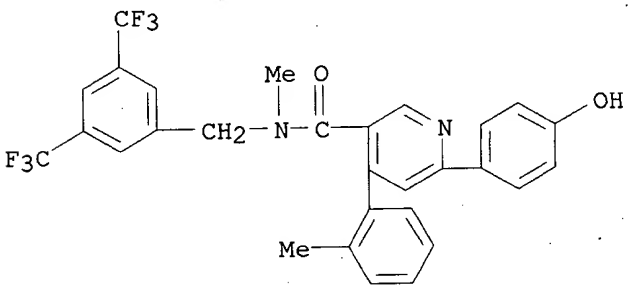
RN 401891-50-7 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(2-hydroxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



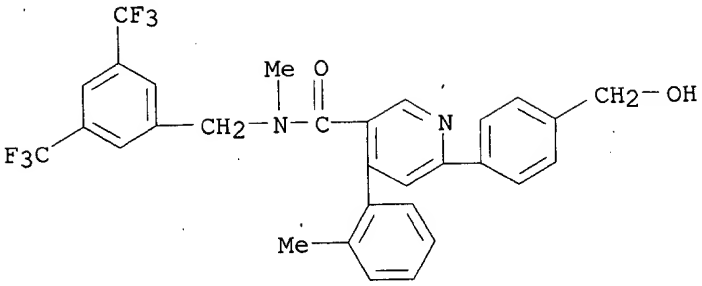
RN 401891-51-8 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(3-hydroxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



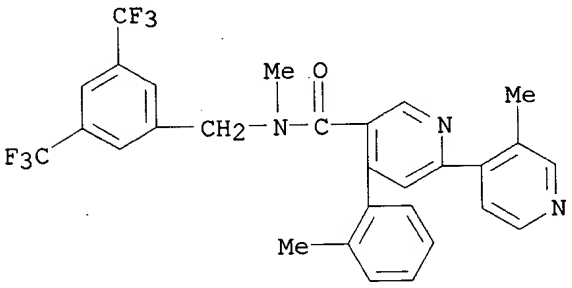
RN 401891-52-9 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-hydroxyphenyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401891-70-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(hydroxymethyl)phenyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

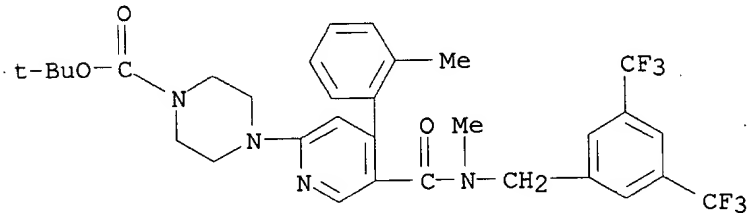


RN 401891-71-2 CAPLUS
CN [2,4'-Bipyridine]-5-carboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N,3'-dimethyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

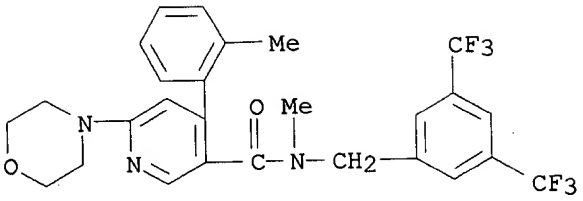


IT **290296-83-2P 290296-89-8P 290296-93-4P**
401892-45-3P 401892-63-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

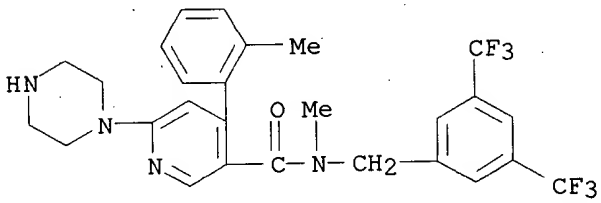
RN 290296-83-2 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



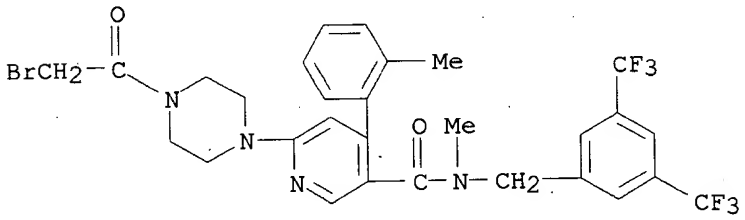
RN 290296-89-8 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



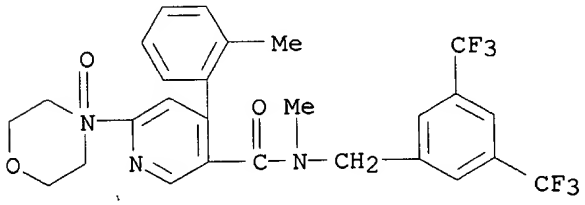
RN 290296-93-4 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



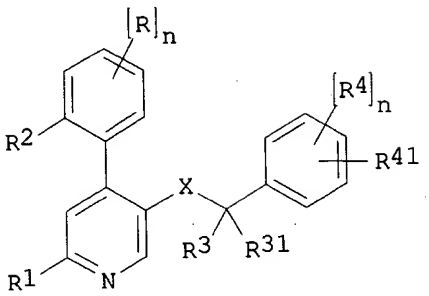
RN 401892-45-3 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(bromoacetyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 401892-63-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)- (9CI) (CA INDEX NAME)



GI



I

AB The title compds. [I; R = H, halo; R1 = (C.tplbond.C)mR11, (CR'=CR'')mR11 (wherein R11 = halo, CN, aryl, etc.; R', R'' = H, OH, alkyl, etc.); R2 = H, alkyl, alkoxy, halo, CF3; R3, R31 = H, alkyl or form together with the C atom to which they are attached a cycloalkyl group; R4, R41 = H, halo, CF3, alkyl, alkoxy; R and R2 or R4 and R41 may be together CH=CHCH=CH, optionally substituted by one or two substituents selected from alkyl, halo or alkoxy; X = CONR8, (CH2)pO, (CH2)pNR8, NR8CO, NR8(CH2)p (wherein R8 = H, alkyl); n = 1-2; m = 0-4; p = 1-2] which are antagonists of the Neurokinin 1 (NK-1, substance P) receptor, and therefore useful in the treatment of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R = H; R1 = N(OH)CH2CH2OH; R2 = Me; R3, R31 = Me; R4 = 3-CF3; R41 = 5-CF3; X = NMeCO] which showed pKi of 9.29 in human NK1 receptor assay, was given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2002:90050 CAPLUS
DN 136:134681
TI Preparation of 4-phenylpyridine derivatives as neurokinin-1 receptor antagonists
IN Hoffmann, Torsten; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002008232	A1	20020131	WO 2001-EP8432	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
			EP 2000-115846 A	20000724
US 2002038030	A1	20020328	US 2001-901311	20010709
			EP 2000-115846 A	20000724
EP 1305319	A1	20030502	EP 2001-960529	20010720

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

EP 2000-115846 A 20000724
WO 2001-EP8432 W 20010720

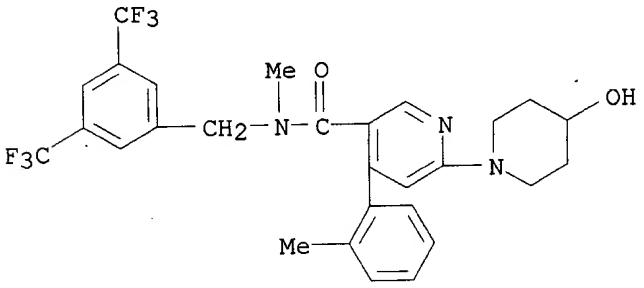
NO 2003000353 A 20030123 NO 2003-353 20030123
EP 2000-115846 A 20000724
WO 2001-EP8432 W 20010720

OS MARPAT 136:134681

IT **393508-72-0P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 393508-72-0 CAPLUS

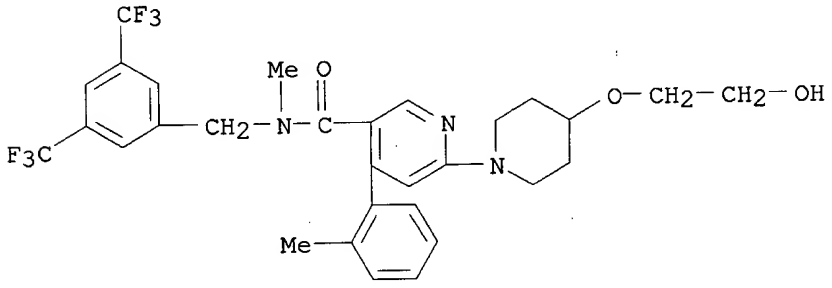
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-hydroxy-1-piperidinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



IT **393508-73-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

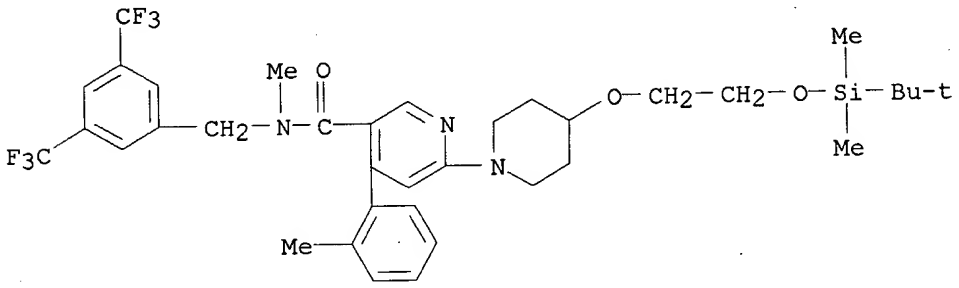
RN 393508-73-1 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethoxy)-1-piperidinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



IT **393508-85-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of 4-phenylpyridines as neurokinin-1 receptor antagonists)

RN 393508-85-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethoxy]-1-piperidinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I or II; R1 = III, 2,3-dihydro-[1,4]oxazin-4-yl, imidazol-1-yl, [1,2,4]triazol-1-yl, NH(CH2)2OH, NR3COCH3, NR3COcyclopropyl; R2 = Me, Cl; R3 = H, Me; R = H, (CH2)2OH; n = 1-2] which have a good affinity of the NK-1 receptor and therefore they may be used in the treatment or prevention of diseases, related to this receptor, were prepd. and formulated. E.g., a multi-step synthesis of I [R1 = [1,2,4]triazol-1-yl; R2 = Me] which showed pKi of 8.4 against binding at human NK1 receptors in CHO cells, was given.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2002:72051 CAPLUS
DN 136:118387
TI Preparation of N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivatives
IN Hoffmann, Torsten; Poli, Sonia Maria; Schnider, Patrick; Sleight, Andrew
PA F. Hoffmann-La Roche A.-G., Switz.
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002006236	A1	20020124	WO 2001-EP7850	20010709

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 2000-115287 A 20000714

EP 1303490 A1 20030423 EP 2001-949475 20010709
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
EP 2000-115287 A 20000714
WO 2001-EP7850 W 20010709

US 2002045642 A1 20020418 US 2001-904059 20010712
EP 2000-115287 A 20000714

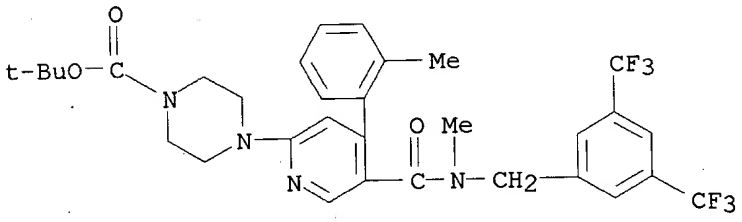
NO 2003000154 A 20030113 NO 2003-154 20030113
EP 2000-115287 A 20000714
WO 2001-EP7850 W 20010709

OS MARPAT 136:118387

IT **290296-83-2P 290296-85-4P 290296-89-8P**
290297-00-6P 290297-11-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate product in prepn. of aminopyridine N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivs.)

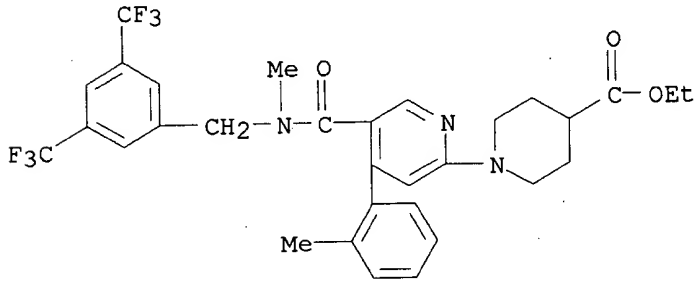
RN 290296-83-2 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



RN 290296-85-4 CAPLUS

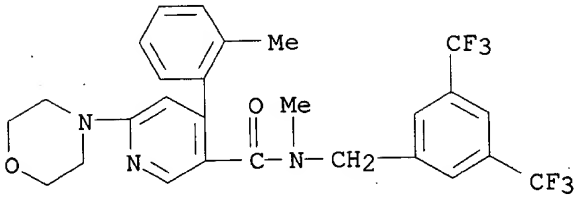
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)



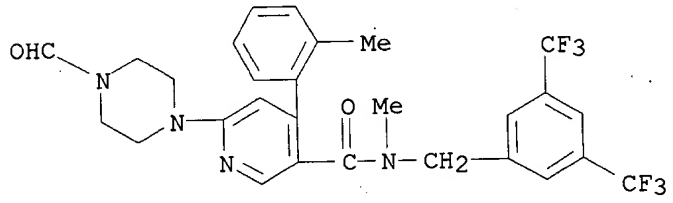
RN 290296-89-8 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-

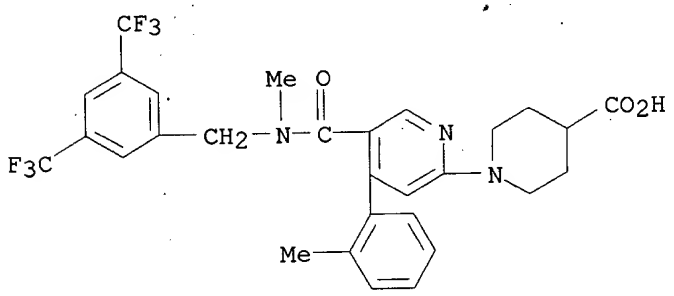
4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



RN 290297-00-6 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

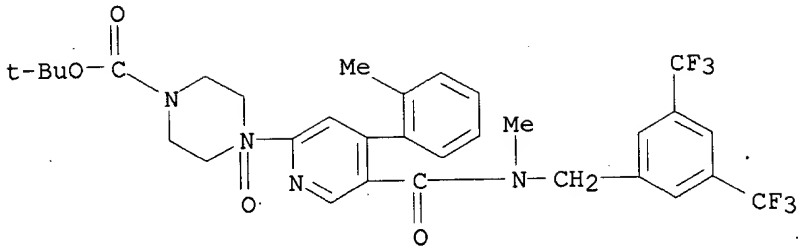


RN 290297-11-9 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)

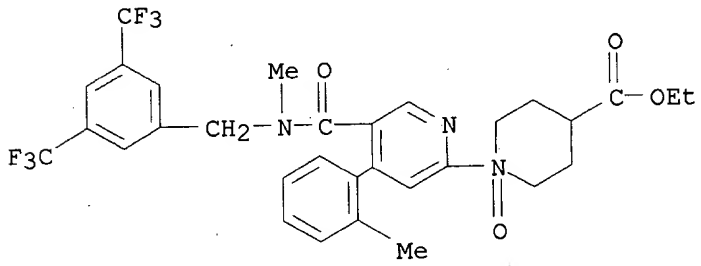


IT **391674-85-4P 391674-86-5P 391674-88-7P**
391674-90-1P 391675-01-7P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminopyridine N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivs.)

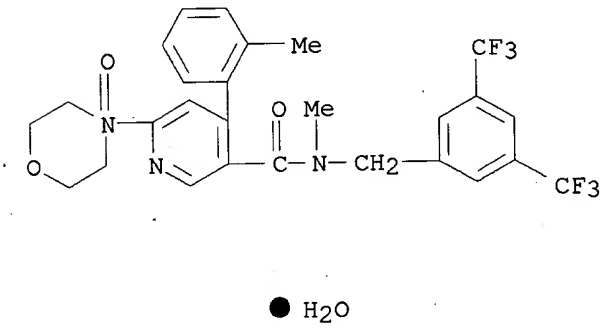
RN 391674-85-4 CAPLUS
CN 1-Piperazinecarboxylic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester, 4-oxide (9CI) (CA INDEX NAME)



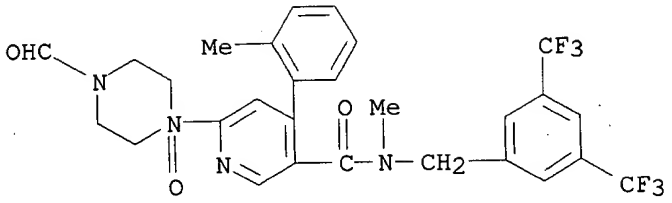
RN 391674-86-5 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester, 1-oxide (9CI) (CA INDEX NAME)



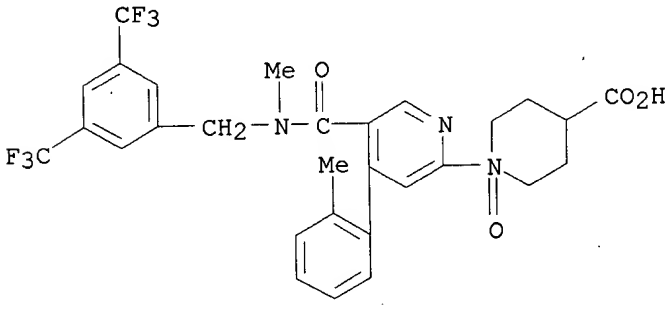
RN 391674-88-7 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-oxido-4-morpholinyl)-, monohydrate (9CI) (CA INDEX NAME)



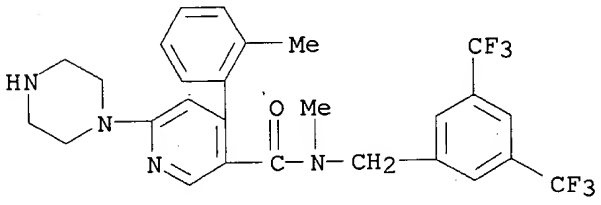
RN 391674-90-1 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-oxido-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 391675-01-7 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1-oxide (9CI) (CA INDEX NAME)



IT **290296-93-4**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant for prepn. of aminopyridine N-oxides as NK1 receptor antagonist prodrugs of 4-phenylpyridine derivs.)
RN 290296-93-4 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



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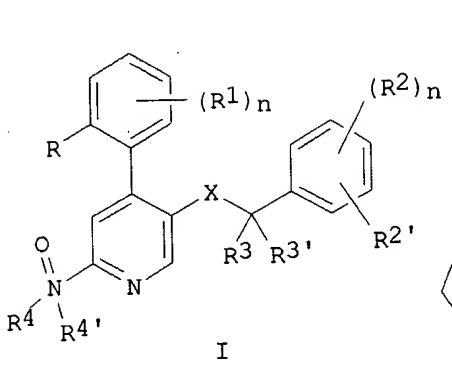

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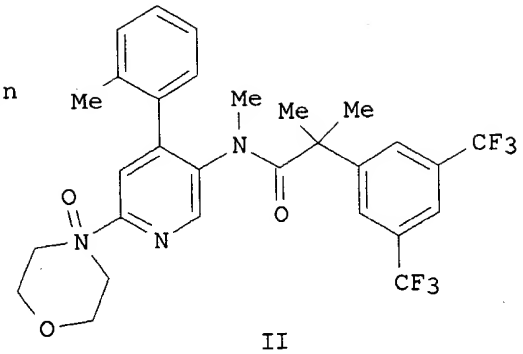


II

AB The prepn. is described for N-oxides (I) wherein R is hydrogen, lower alkyl, lower alkoxy, or trifluoromethyl; R1 is hydrogen or halogen; or R and R1 may be together with the ring carbon atoms to which they are attached -CH=CH-CH=CH-; R2 and R2' are independently from each other hydrogen, halogen, trifluoromethyl, lower alkoxy or cyano; or R2 and R2' may be together -CH=CH-CH=CH-, optionally substituted by one or two substituents selected from lower alkyl or lower alkoxy; R3, R3' are independently from each other hydrogen, lower alkyl or cycloalkyl; R4, R4' are independently from each other -(CH2)mOR6 or lower alkyl; or R4 and R4' form together with the N-atom to which they are attached a cyclic tertiary amine with substituent R5 chosen from hydrogen, hydroxy, lower alkyl, -lower alkoxy, -(CH2)mOH, -COOR3, -CON(R3)2,-N(R3)CO-lower alkyl or -C(O)R3; R6 is hydrogen, lower alkyl or phenyl; X is -C(O)N(R6)-, -N(R6)C(O)-, -(CH2)mO- or -O(CH2)m-; n is 0, 1, 2, 3 or 4 and; m is 1, 2, or 3; and to their pharmaceutically acceptable acid addn. salts. These compds. may be uses as prodrugs for the treatment or prevention of illnesses, related to the NK1 receptor. Thus, 2-[3,5-bis(trifluoromethyl)phenyl]-N-methyl-N-[6-(4-oxymorpholin-4-yl)-4-o-tolylpyridin-3-yl]isobutyramide (II) and related compds. were prepd. in multistep procedures.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2001:396485 CAPLUS
DN 135:5533
TI Process for preparation of pyridine derivatives
IN Hilpert, Hans; Hoffmann-Emery, Fabienne; Rimmler, Goesta; Rogers-Evans, Mark; Stahr, Helmut Werner; Waldmeier, Pius
PA F. Hoffmann-La Roche A.-G., Switz.
SO Eur. Pat. Appl., 28 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1103546	A1	20010530	EP 2000-125665	20001123
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
				EP 1999-123686 A	19991129

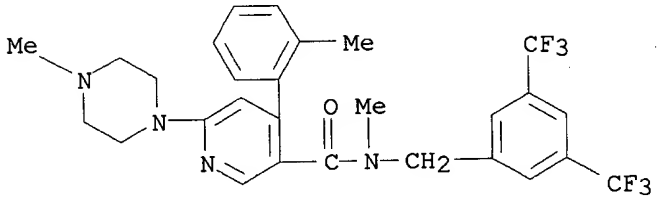
US 6303790	B1	20011016	US 2000-716538 20001120 EP 1999-123686 A 19991129
JP 2001151755	A2	20010605	JP 2000-360682 20001128
JP 3403164	B2	20030506	EP 1999-123686 A 19991129
CN 1297887	A	20010606	CN 2000-128383 20001128 EP 1999-123686 A 19991129

OS CASREACT 135:5533; MARPAT 135:5533

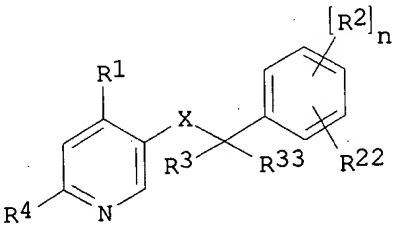
IT **290297-57-3P**
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(process for prepn. of pyridine derivs.)

RN 290297-57-3 CAPLUS

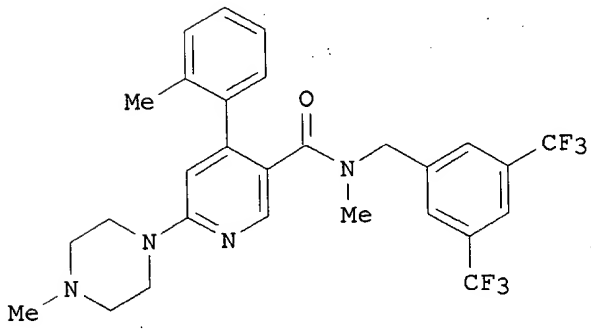
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



GI



I



II

AB The title compds. [I; R1 = alkyl, (un)substituted aryl; R2, R22 = H, halo,

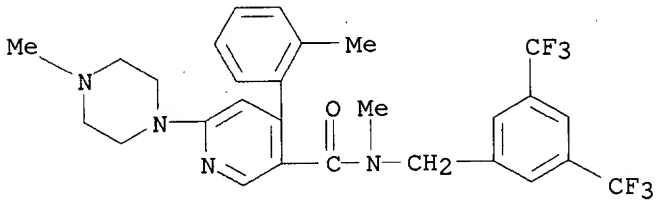
CN 1270959	A	20001025	CN 2000-102401 20000223 EP 1999-103504 A 19990224 EP 1999-123689 A 19991129
ES 2171109	A1	20020816	ES 2000-418 20000223 EP 1999-103504 A 19990224 EP 1999-123689 A 19991129
JP 2000247957	A2	20000912	JP 2000-47003 20000224 EP 1999-103504 A 19990224 EP 1999-123689 A 19991129
BG 104187	A	20001130	BG 2000-104187 20000224 EP 1999-103504 A 19990224 EP 1999-123689 A 19991129
US 2002091265	A1	20020711	US 2001-901982 20010710
US 6479483	B2	20021112	EP 1999-103504 A 19990224 EP 1999-123689 A 19991129 US 2000-507456 A320000222

OS MARPAT 133:207811

IT **290296-52-5P 290296-83-2P 290296-84-3P**
290296-85-4P 290296-86-5P 290296-89-8P
290296-93-4P 290296-94-5P 290296-95-6P
290296-96-7P 290296-98-9P 290296-99-0P
290297-00-6P 290297-11-9P 290297-12-0P
290297-57-3P 290297-60-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-benzyl-4-tolylnicotinamides and related compds. as neurokinin-1 receptor antagonists)

RN 290296-52-5 CAPLUS

CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 290296-83-2 CAPLUS

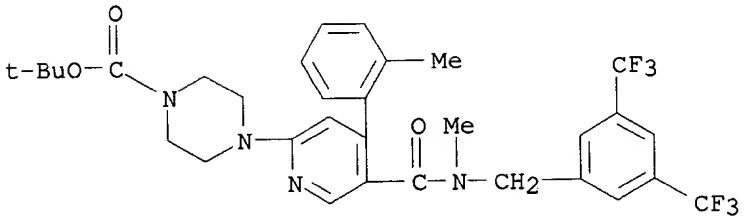
CN 1-Piperazinecarboxylic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

CF3, etc.; R2 and R22 may be together = (un)substituted CH:CHCH:CH; R3, R33 = H, alkyl, or forming a cycloalkyl together with the carbon atom, to which they are attached; R4 = H, alkyl, (un)substituted NH2, etc.; X = CONR5, NR5CO; R5 = H, alkyl, CH2Ph; n = 0-4], useful as antagonists of neurokinin 1 receptor (no data), were prepd. Thus, treating 6-chloronicotinic acid with SOCl2 and MeNH2.HCl followed by reaction of 6-chloro-N-methylnicotinamide with o-tolylmagnesium chloride and 1-methylpiperazine, treatment of 6-(4-methylpiperazin-1-yl)-4-o-tolyl-4,5-dihydropyridine-3-carboxylic acid methylamide with MnO2, and reacting N-methyl-6-(4-methylpiperazin-1-yl)-4-o-tolylnicotinamide with 3,5-bis(trifluoromethyl)benzyl bromide afforded the nicotinamide II.

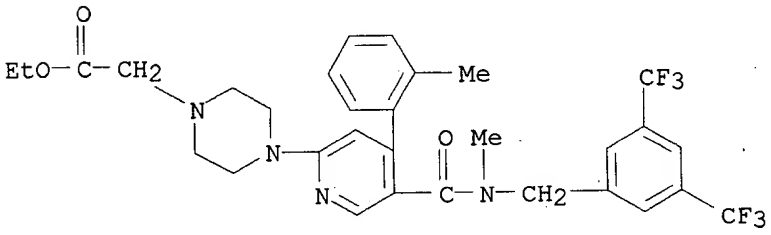
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS
AN 2000:607348 CAPLUS
DN 133:207811
TI Preparation of N-benzyl-4-tolylnicotinamides and related compounds as neurokinin-1 receptor antagonists.
IN Boes, Michael; Branca, Quirico; Galley, Guido; Godel, Thierry; Hoffmann, Torsten; Hunkeler, Walter; Schnider, Patrick; Stadler, Heinz
PA F. Hoffmann-La Roche Ag, Switz.
SO Ger. Offen., 38 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

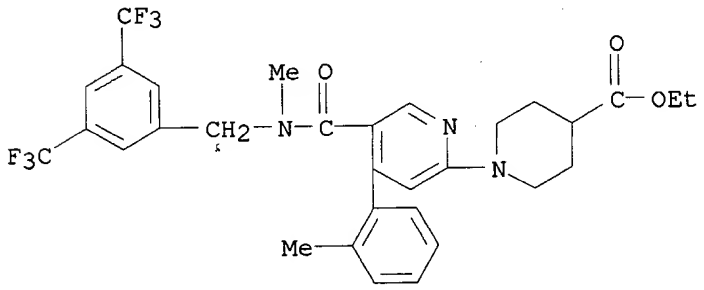
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 10008042	A1	20000831	DE 2000-10008042	20000222
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
EP 1035115	A1	20000913	EP 2000-102260	20000215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
GB 2347422	A1	20000906	GB 2000-3908	20000218
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
NZ 502948	A	20010928	NZ 2000-502948	20000218
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
FR 2790473	A1	20000908	FR 2000-2170	20000222
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
US 6297375	B1	20011002	US 2000-507456	20000222
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
ZA 2000000894	A	20000824	ZA 2000-894	20000223
			EP 1999-103504 A	19990224
NO 2000000885	A	20000825	NO 2000-885	20000223
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129
BR 2000000908	A	20000912	BR 2000-908	20000223
			EP 1999-103504 A	19990224
			EP 1999-123689 A	19991129



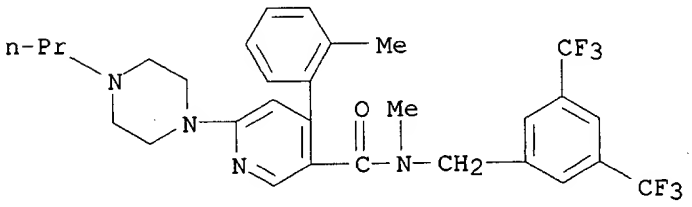
RN 290296-84-3 CAPLUS
CN 1-Piperazineacetic acid, 4-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)

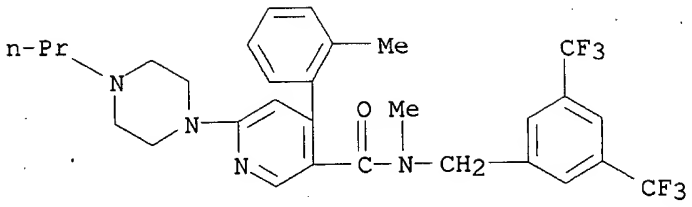


RN 290296-85-4 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)

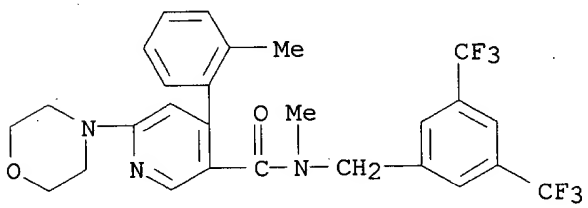


RN 290296-86-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-propyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

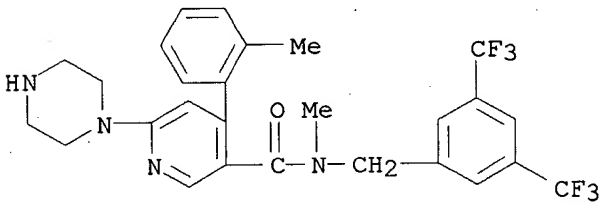




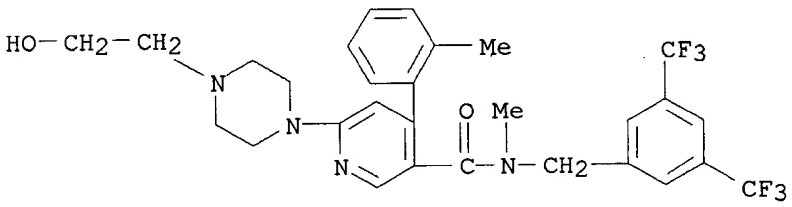
RN 290296-89-8 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-morpholinyl)- (9CI) (CA INDEX NAME)



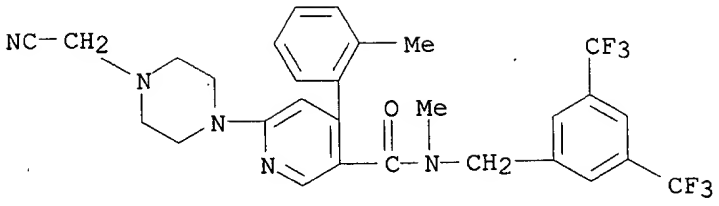
RN 290296-93-4 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(1-piperazinyl)- (9CI) (CA INDEX NAME)



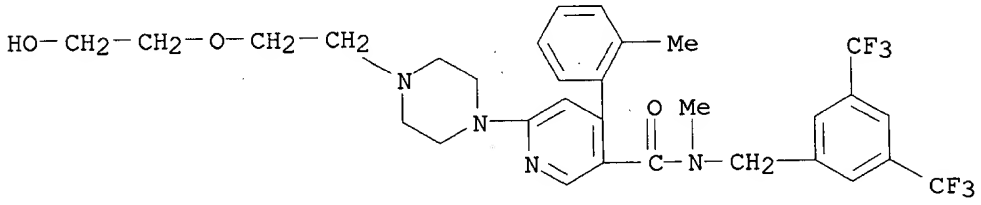
RN 290296-94-5 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(2-hydroxyethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



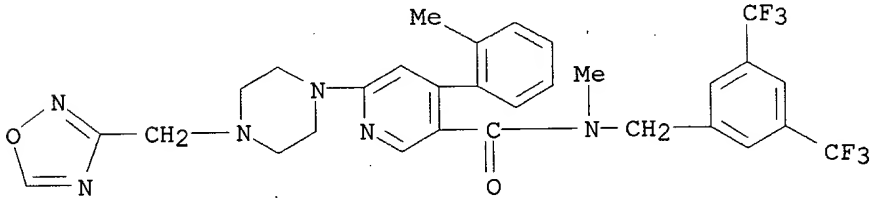
RN 290296-95-6 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-(cyanomethyl)-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



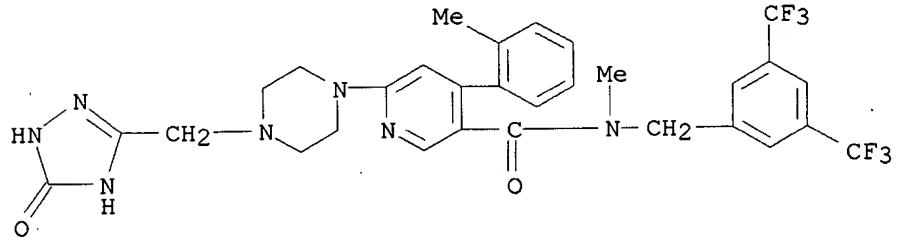
RN 290296-96-7 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



RN 290296-98-9 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-[4-(1,2,4-oxadiazol-3-ylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

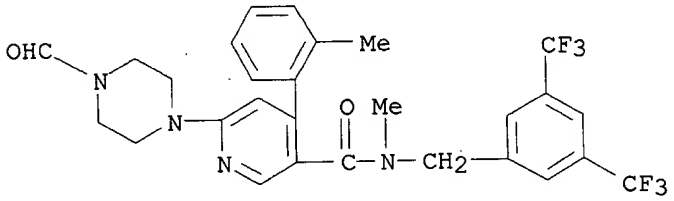


RN 290296-99-0 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-[4-[(2,5-dihydro-5-oxo-1H-1,2,4-triazol-3-yl)methyl]-1-piperazinyl]-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

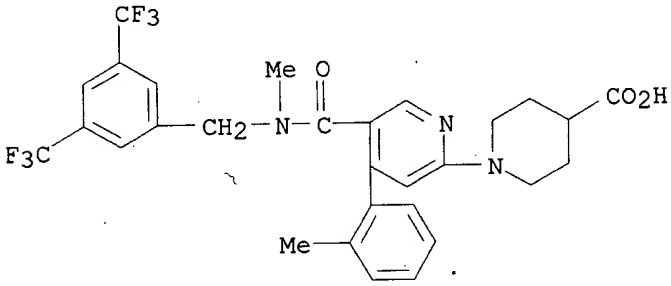


RN 290297-00-6 CAPLUS

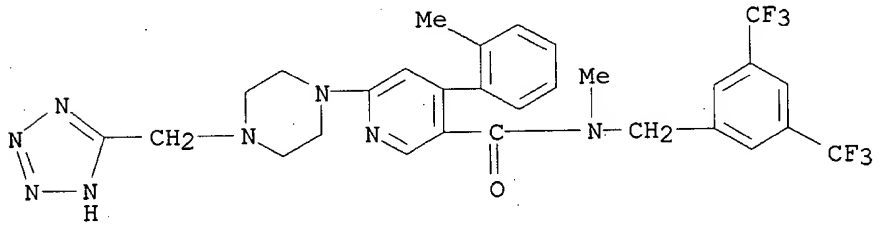
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-6-(4-formyl-1-piperazinyl)-N-methyl-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



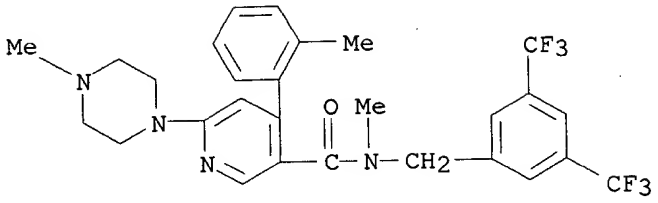
RN 290297-11-9 CAPLUS
CN 4-Piperidinecarboxylic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]- (9CI) (CA INDEX NAME)



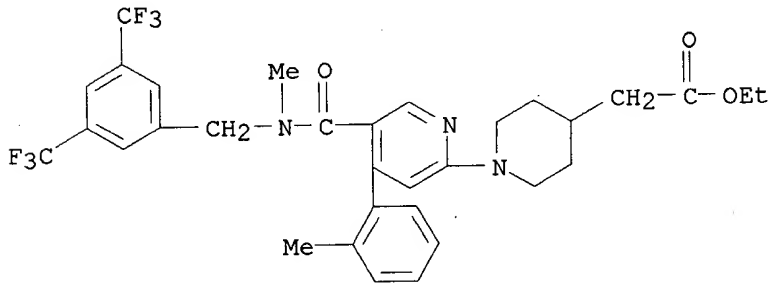
RN 290297-12-0 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-[4-(1H-tetrazol-5-ylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 290297-57-3 CAPLUS
CN 3-Pyridinecarboxamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-N-methyl-4-(2-methylphenyl)-6-(4-methyl-1-piperazinyl)- (9CI) (CA INDEX NAME)



RN 290297-60-8 CAPLUS
CN 4-Piperidineacetic acid, 1-[5-[[[[3,5-bis(trifluoromethyl)phenyl]methyl]methylamino]carbonyl]-4-(2-methylphenyl)-2-pyridinyl]-, ethyl ester (9CI) (CA INDEX NAME)



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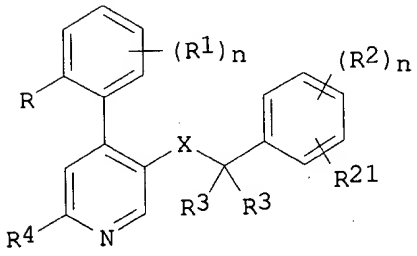

I

AB Title compds. [I; R = H, alkyl, alkoxy, halo, CF3; R1 = H, halo; RR1 = CH:CHCH:CH; R2, R21 = H, halo, CF3, alkoxy, cyano; R2R21 = (substituted) CH:CHCH:CH; R3 = H, alkyl, cycloalkyl; R4 = H, N(R5)2, N(R5)(CH2)nOH, N(R5)S(O)2A, N(R5)S(O)2Ph, N:CHN(R5)2, N(R5)C(O)R5, specified cyclic tertiary amine; R5 = H, cycloalkyl, benzyl, alkyl; X = C(O)N(R5), (CH2)mO, (CH2)mN(R5), N(R5)C(O), N(R5)(CH2)m; n = 0-4; m = 1, 2], were prepd. Thus, 4-o-tolylnicotinic acid (prepn. given) was stirred with SOCl2 and cat. DMF in CH2Cl2 to give a residue which was refluxed with N-[3,5-bis(trifluoromethyl)benzyl]-N-methylamine and Et3N in PhMe to give 67% N-(3,5-bistrifluoromethylbenzyl)-N-methyl-4-o-tolylnicotinamide. Tested I antagonized NK-1 receptors with pKi = 8.20-9.54.

=> d his

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L1                STRUCTURE UPLOADED
L2              6 S L1
L3             39 S L1 SSS FULL

     FILE 'CAPLUS' ENTERED AT 08:43:57 ON 24 MAY 2003
L4              7 S L3

=> d cost
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CONNECT CHARGES                                         0.68       1.17
NETWORK CHARGES                                         0.12       0.24
SEARCH CHARGES                                          0.00     147.75
DISPLAY CHARGES                                        30.24      30.24
                                                    -------    -------
                                                       31.04     179.40
CAPLUS FEE (5%)                                         1.55       1.55
                                                    -------    -------
FULL ESTIMATED COST                                    32.59     180.95

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -4.56      -4.56

IN FILE 'CAPLUS' AT 08:45:05 ON 24 MAY 2003
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